Evaluation of the Micral-Test ® S, a Qualitative Immunologic Patient Self-test for Microalbuminuria: the PROSIT Project

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Introduction

Diabetic nephropathy is associated with increased morbidity and mortality and impaired quality of life for people with diabetes and a financial burden for health care systems. Between 30 and 50 % of all patients on chronic dialysis in Western countries are diabetic, and, with the increasing incidence of diabetes and its associated life expectancy, this percentage is growing.[1]

Microalbuminuria is defined as an elevated urinary albumin excretion of 20–200 μg min^{-1} or 30–300 mg 24 h^{-1} in overnight or 24 h urine collections or elevated albumin concentration of 20–200 mg l^{-1} in early morning urine. Persistent microalbuminuria is not only predictive for the development of overt diabetic nephropathy in both Type 1[2] and Type 2 diabetes,[3] but is also a strong predictor for other diabetes-related complications and cardiovascular excess mortality in both types of diabetes[3–5] and non-diabetic subjects.[6] Despite high prevalences of raised urinary albumin concentration both in Type 1 and Type 2 diabetes (up to 35 %),[7,8] so far even in countries who can afford it, screening programmes for diabetic nephropathy are not realized. In Germany only a minority of the diabetic patients is regularly screened for microalbuminuria.[9] Therefore the PROSIT Project (Proteinuria Screening and Intervention Project) was initiated, to implement the St Vincent Declaration Action Programme[10] by developing and implementing easy screening concepts for diabetic nephropathy. Part of this project was the evaluation of the newly developed qualitative immunologic self-test Micral-Test ® S.

Patients and Methods

Patients

Within a period of 2 months in a university hospital and a city hospital in Munich, all consecutive unselected diabetic patients were asked to take part in the study. Exclusion criteria included: ketoacidosis; known kidney disease; serum creatinine above 132.7 μmol l^{-1}; evidence of urinary tract infection; fever $>$ 38°C; severe heart insufficiency NYHA III or IV; menstruation or antibiotic therapy. A total of 108 patients were included. Clinical data are depicted in Table 1.

Methods

Patients received urine jars, test-strips and information material, and performed self-tests for microalbuminuria on a first morning urine on three days within one week.

Table 1. Clinical characteristics of the patient sample

Total (n = 108)	Type 1 diabetes (n = 58)	Type 2 diabetes (n = 50)
Age (yr)	31 ± 13	59 ± 10
Gender (male/female)	26/32	23/27
Known duration of diabetes (yr)	13 ± 12	8 ± 7

Values are ×±SD.

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The qualitative self-test Micral-Test ® S uses antibodies labelled with colloidal gold. The reaction is complete after approximately 45 s; the reaction colour should be read after 60 s and remains stable up to 5 min. The comparison colours given on the tube label correspond to < 10 mg l^{-1} (negative) and ≥ 20 mg l^{-1} (positive). The patients documented each test result as either 'negative' or 'positive'. Based on all three single test results overall results were assessed under two different assumptions: a positive microalbuminuria by self-test was assumed either by at least one positive test out of three self-tests, or in case of at least two positive self-tests. The same urine specimens were retested using quantitative measurement of urinary albumin concentration by immunoturbidimetry.[11] A positive overall retest result was defined as more than 20 mg l^{-1} albumin in at least two urine samples. Sensitivity, specificity, positive and negative predictive values were calculated for both ways of assessing a positive self-test.

Results

Using the quantitative measurement of the urinary albumin concentration by immunoturbidimetry as a reference method, the following results were obtained. If one positive out of three self-tests per week was considered as a positive overall self-test, the sensitivity of the self-test was 90 %, specificity 77 %, positive predictive value 49 % and negative predictive value 97 %. 79.6 % of patients classified themselves correctly (percentage of true positive plus true negative results; Table 2(a)). When at least two positive self-tests were considered necessary for the definition of a positive self-test, sensitivity decreased to 81 % and negative predictive value was 95 %, whereas specificity increased to 92 % and positive predictive value to 71 %; 89.8 % of all patients classified themselves correctly (Table 2(b)).

Table 2. Agreement between overall self-test results (MicralTest ® S) and overall quantitative retest results (immunoturbidimetry). (a) Version 1: overall positive self-test defined as at least one positive out of three self-tests per week. (b) Version 2: overall positive self-test defined as at least two positive out of three self-tests per week

		Overall qualitative self-test result		
		Negative	Positive	Total
(a) Version 1				
Overall semi-quantitative retest result	Negative	67	20	87
	Positive	2	19	21
	Total	69	39	108
(b) Version 2				
Overall semi-quantitative retest result	Negative	80	7	87
	Positive	4	17	21
	Total	84	24	108

Discussion

Despite the recommendations in the consensus guidelines for the management of Type 1[12] and Type 2 diabetes,[13] in Germany only a minority of diabetic patients are screened annually for diabetic nephropathy. Because of this and to give the patients self-responsibility in the field of diabetic nephropathy, the qualitative self-test for microalbuminuria Micral Test ® S was developed. In this study its accuracy has been assessed for the first time. Sensitivity and specificity were found to be sufficiently high for screening purposes (81 % and 92 %, respectively), especially considering that without self-testing a large proportion of the diabetic patients would not be screened at all. Moreover self-testing is not expensive. Our data suggest that the assessment of a positive self-test should be based on at least two positive out of three single test results in order to increase the diagnostic value. To overcome the influence of exercise, posture and diet, the early morning urine should be analysed. Because of considerable intra-individual variations of urinary albumin excretion,[14] three self-tests for microalbuminuria should be performed, for practical reasons preferably within 1 week. Positive self-test results must be confirmed by a quantitative method. If a persistent microalbuminuria is detected and confounders ruled out by further diagnostic measures, the diagnosis of incipient nephropathy should be confirmed and an intervention should start.

Our data indicate that the accuracy of the Micral Test ® S is sufficient for its use in screening programmes for diabetic nephropathy. The time has come to give patients self-responsibility not only in the field of blood glucose, urinary glucose, ketonuria, and blood pressure monitoring, but also in early detection of diabetic nephropathy.

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